

## Multidrug-Resistant *Salmonella enterica* Serotype Typhimurium DT104

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### To the Editor:

Molbak et al. (Nov. 4 issue) (1) call attention to disparities between the results of in vitro tests of ciprofloxacin sensitivity in salmonella and treatment failure. The evolution of antibiotic resistance most often occurs in vivo, and some resistance factors may be promoted by this environment. Exciting results have emerged from the application of in vivo expression technology (IVET) to the discovery of virulence factors. (2) In many of those experiments, antibiotic resistance has been used as a reporting mechanism for IVET-related gene expression. This approach might obscure the possibility that resistance itself may sometimes be an in vivo-limited virulence factor in nature. This concept might be important in the evaluation of candidate drugs for the emergence of resistance, in research on the mechanism of resistance, and as a reminder to be cautious in interpreting the predictive value of in vitro tests for antibiotic susceptibility.

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### References

1. Molbak K, Baggesen DL, Aarestrup FM, et al. An outbreak of multidrug-resistant, quinolone-resistant *Salmonella enterica* serotype typhimurium DT104. N Engl J Med 1999;341:1420-5.

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2. Mahan MJ, Tobias JW, Slauch JM, Hanna PC, Collier RJ, Mekalanos JJ. Antibiotic-based selection for bacterial genes that are specifically induced during infection of a host. Proc Natl Acad Sci U S A 1995;92:669-73.

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### The authors reply:

### To the Editor:

We agree with Dr. Lederberg that the concept of genes induced in vivo is exciting and may be important for a more complete understanding of factors that contribute to the virulence and antimicrobial-drug resistance of bacterial pathogens. In addition, disparities between the results of in vitro tests of ciprofloxacin sensitivity and reduced treatment efficacy in vivo may be related to a number of other factors, including pharmacokinetics, the distribution of the drug in various tissue compartments, and the binding of active substances to organic matter in the gut. That the issue regarding the relevant in vitro cutoff point for the minimal inhibitory concentration of ciprofloxacin that can be used to discriminate between sensitive and resistant salmonella is controversial most probably reflects the fact that there has been little experimental or observational therapeutic evidence in the case of zoonotic salmonella strains containing a single mutation in a gyrase gene.

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